

XX PS Claim 13; Page 203; 236pp; English.

CC This is an immunodominant peptide epitope from the M. tuberculosis 32A

CC kD protein. Sequences shown in AAW75642 to AAW75698 represent synthetic

CC peptides derived from the native 32A kD major secretory protein of

CC Mycobacterium tuberculosis. These peptides are used for identifying the

CC immunodominant T-cell epitope of the 32A kD protein. The invention

CC provides an agent for vaccinating mammals against Mycobacterium. The

CC agent comprises at least one of the major abundant extracellular 110, 80,

CC 71, 58, 45, 32A, 32B, 30, 24, 23.5, 23, 16, 14 or 12 kD proteins of M.

CC interleukin-12 (IL-12) or MF59 as adjuvants. The agent containing the

CC nucleic acid encoding the extracellular products are used to raise a

CC protective or therapeutic immune response against Mycobacterium.

CC specifically M. tuberculosis. The immunodominant epitopes can also be

CC used (typically in a cutaneous hypersensitivity test) to detect an immune

CC response to vaccination. Preparation of the agent does not require

CC selection of the most immunogenic products, so large scale production and

CC purification are easy, resulting in a consistent, standardised

CC formulation, having lower toxicity than killed or attenuated vaccines.

CC The agents provide a rapid and effective response (including a strong

CC cell-mediated component) and are safe even in immunocompromised subjects.

CC They prevent development of an opsonising humoral response that might

CC spread intracellular pathogens.

XX SQ Sequence 15 AA;

Query Match 100.0%; Score 84; DB 19; Length 15;

Best Local Similarity 100.0%; Pred. No. 2.7e-08;

Matches 15; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 GLRAQDDFGWDINT 15

Db 1 glraqddfgwdint 15

RESULT 2

AA11298

ID AAR11298 standard; Protein; 20 AA.

AC AAR11298;

XX 30-MAY-1991 (first entry)

XX Recombinant 36-55 antigenic peptide from M. tuberculosis 32kD Ag.

XX tuberculosis; vaccine; BCG; 32kD antigen.

OS Mycobacterium tuberculosis.

XX EP419355-A.

XX 27-MAR-1991.

XX 19-SEP-1990; 90EP-0402590.

XX 19-SEP-1989; 89EP-0402571.

XX 19-SEP-1990; 90EP-0402590.

XX (INNO-) INNOGENETICS NV SA.

XX Content J, De Wit L, De Bruyn J, Van Vooren JP;

XX WPI; 1991-088933/13.

XX Polypeptide comprising recombinant polypeptide - with defined

XX peptide sequence(s) used for diagnosis and for preparing vaccine

XX against tuberculosis

PS Claim 45; Page 72; 134pp; English.

XX

Thu

CC This peptide corresponds to amino acids 36 to 55 of mature 32kD

CC antigen of M. tuberculosis. It is used to produce antibodies,

CC particularly monoclonal antibodies, for the diagnosis of evolutive

CC tuberculosis.

CC See also AAQ11081-3, AAQ11086-Q11090, AAQ11101-8, AAR11297,

CC AAR11299-R11304.

SQ Sequence 20 AA;

Query Match 100.0%; Score 84; DB 12; Length 20;

Best Local Similarity 100.0%; Pred. NO. 3.8e-08;

Matches 15; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

QY 1 GLRAQDDFGWDINT 15

Db 6 glraqddfgwdint 20

RESULT 3

AA196926

ID AAY96926 standard; Protein; 302 AA.

XX AAY96926;

XX 31-OCT-2000 (first entry)

XX M. tuberculosis antigen 85A.

XX Interleukin 12; IL-12; gamma-interferon; antigen; stimulate;

XX immunostimulant; immunomodulatory; secretory protein.

XX Mycobacterium tuberculosis.

XX WO200039301-A2.

XX 06-JUL-2000.

XX 23-DEC-1999; 99WO-US30975.

XX 24-DEC-1998; 98US-0220416.

XX (CORI-) CORIXA CORP.

XX Skeiky Y;

XX WPI; 2000-452399/39.

XX N-PSDB; AA53601.

XX Potentiating immune responses to antigens using specified Mycobacterium

XX tuberculosis proteins

XX Claim 1; Fig 4B; 30pp; English.

XX The Mycobacterium tuberculosis proteins encoded by AAW53599-603

XX stimulate interleukin (IL)-12 and gamma-interferon production. A number

XX of cloned M. tuberculosis antigens were expressed as recombinant proteins

XX in Escherichia coli. After purification, these proteins were tested for

XX their ability to stimulate the production of IL-12 by a mouse macrophage

XX cell line, RAW264. The concentrations of IL-12 in RAW264 culture

XX supernatants were measured by an ELISA using an antibody to detect the

XX p40 component of the IL-12. Among the 18 proteins tested, only 2,

XX designated DPV and DPAS stimulated the production of IL-12. The

XX stimulatory activities of these proteins were not affected by the

XX inclusion of polymixin B in the cultures, which abrogated the IL-12

XX stimulatory activities of lipopolysaccharide, a polyclonal B-cell

XX mitogen. Both DPV and DPAS are secretory proteins of M. tuberculosis.

XX A method of using the M. tuberculosis proteins to induce and potentiate

XX immune reactions to antigens is claimed.

SQ Sequence 302 AA;

XX Claim 13; Page 203; 236pp; English.
 XX This is an immunodominant peptide epitope from the M. tuberculosis 32A
 CC KD protein. Sequences shown in AAW75642 to AAW75698 represent synthetic
 CC peptides derived from the native 32A kD major secretory protein of
 CC Mycobacterium tuberculosis. These peptides are used for identifying the
 CC immunodominant T-cell epitope of the 32A kD protein. The invention
 CC provides an agent for vaccinating mammals against Mycobacterium. The
 CC agent comprises at least one of the major abundant extracellular 110, 80,
 CC 71, 58, 45, 32A, 32B, 30, 24, 23.5, 23, 16, 14 or 12 kD proteins of M.
 CC tuberculosis, or at least 1 of their immunodominant epitopes and
 CC interleukin-12 (IL-12) or MF59 as adjuvants. The agent containing the
 CC nucleic acid encoding the extracellular products are used to raise a
 CC protective or therapeutic immune response against Mycobacterium,
 CC specifically M. tuberculosis. The immunodominant epitopes can also be
 CC used (typically in a cutaneous hypersensitivity test) to detect an immune
 CC response to vaccination. Preparation of the agent does not require
 CC selection of the most immunogenic products, so large scale production and
 CC purification are easy, resulting in a consistent, standardised
 CC formulation, having lower toxicity than killed or attenuated vaccines.
 CC The agents provide a rapid and effective response (including a strong
 CC cell-mediated component) and are safe even in immunocompromised subjects.
 CC They prevent development of an opsonising humoral response that might
 CC spread intracellular pathogens.
 XX
 XX Sequence 15 AA;

Query Match 100.0%; Score 88; DB 19; Length 15;
 Best Local Similarity 100.0%; Pred. No. 6.7e-07;
 Matches 15; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 CGNGKPSDLGGNNLP 15
 DB 1 CGNGKPSDLGGNNLP 15

RESULT 2
 AAW63038
 ID AAW63038 standard; peptide; 17 AA.
 XX
 AC AAW63038;
 XX
 DT 23-OCT-1998 (first entry)
 XX
 DE M. tuberculosis 32A kD protein derived peptide 43A (residues 211-227).
 XX
 KW Mycobacterium tuberculosis; vaccination; extracellular product;
 KW Immunodominant epitope; interleukin-12; MF59; immune response;
 KW opsonising humoral response; intracellular pathogen.
 XX
 OS Synthetic.
 OS Mycobacterium tuberculosis.
 XX
 PN WO9831388-A1.
 XX
 PD 23-JUL-1998.
 XX
 PF 15-JAN-1998; 98WO-US00942.
 XX
 PR 21-JAN-1997; 97US-0786533.
 XX
 PA (REGC) UNIV CALIFORNIA.
 XX
 PI Harth G, Horwitz MA, Lee B;
 XX
 DR WPI; 1998-413815/35.
 XX
 XX Vaccines against Mycobacterium containing major extracellular
 PT proteins - used to, e.g. induce protective and therapeutic immune
 PT responses, and for detecting an immune response

PS Example 29; Page 101; 236pp; English.
 XX represents a synthetic peptide derived from the
 CC secretory protein of M. tuberculosis. This is an
 CC immunodominant T-cell epitope of the 32A kD pro
 CC provides an agent for vaccinating mammals again
 CC agent comprises at least one of the major abund
 CC 80, 71, 58, 45, 32A, 32B, 30, 24, 23.5, 23, 1
 CC M. tuberculosis, or at least 1 of their immun
 CC interleukin-12 (IL-12) or MF59 as adjuvants. Th
 CC nucleic acid encoding the extracellular produ
 CC protective or therapeutic immune response again
 CC specifically M. tuberculosis. The immunodomin
 CC used (typically in a cutaneous hypersensitivity
 CC immune response to vaccination. Preparation of
 CC selection of the most immunogenic products, so
 CC purification are easy, resulting in a consist
 CC formulation, having lower toxicity than killed
 CC The agents provide a rapid and effective respo
 CC cell-mediated component) and are safe even in
 CC They prevent development of an opsonising humo
 CC spread intracellular pathogens.
 XX
 XX Sequence 17 AA;

Query Match 100.0%; Score 88; DB 19;
 Best Local Similarity 100.0%; Pred. No. 7.6e-
 Matches 15; Conservative 0; Mismatches

OY 1 CGNGKPSDLGGNNLP 15
 DB 1 CGNGKPSDLGGNNLP 15

RESULT 3
 AAR11302
 ID AAR11302 standard; Protein; 20 AA.

XX AAR11302;
 AC
 DT 30-MAY-1991 (first entry)
 XX
 DE Recombinant 211-230 antigenic peptide from M.
 XX
 KW tuberculosis; vaccine; BCG; 32kD antigen.
 XX
 OS Mycobacterium tuberculosis.
 XX
 PN EP419355-A.
 XX
 PD 27-MAR-1991.
 XX
 PF 19-SEP-1990; 90EP-0402590.
 XX
 PR 19-SEP-1989; 89EP-0402571.
 PR 19-SEP-1990; 90EP-0402590.
 XX
 PA (INNO-) INNOGENETICS NV SA.
 XX
 PI Content J, De Wit L, De Bruyn J, Van Voore
 XX
 DR WPI; 1991-088933/13.
 XX
 PT Polypeptide comprising recombinant polypeptid
 PT peptide sequence(s) used for diagnosis and fc
 PT against tuberculosis
 XX
 PS Claim 45; Page 72; 134pp; English.
 XX
 CC This peptide corresponds to amino acids 211 t
 CC antigen of M. tuberculosis. It is used to prod
 CC particularly monoclonal antibodies, for the di

kD major
 identifying the
 invention
 erium. The
 cellular 110,
 kD proteins of
 types and
 raising the
 to raise a
 rium,
 can also be
 ect an
 es not require
 production and
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 i vaccines.
 ing a strong
 mised subjects.
 that might

0; Gaps 0;

kD Ag.

line

32kD

ative

De

CC tuberculosis.

CC See also AAQ11081-3, AAQ11086-Q11090, AAQ11101-8, AAQ11297-R11301,

CC AAQ11303-4.

XX

SQ Sequence 20 AA;

Query Match

Best Local Similarity 100.0%; Score 88; DB 12; Length 20;

Matches 15; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 CGNGKPSDLGNNLP 15

|||||

Db 1 cngkpsdlggnlp 15

RESULT 4

AAQ96926

ID AAQ96926 standard; Protein; 302 AA.

XX

AC AAQ96926;

XX

DT 31-OCT-2000 (first entry)

XX

DE M. tuberculosis antigen 85A.

XX

KW Interleukin 12; IL-12; gamma-interferon; antigen; stimulate;

KW immunostimulant; immunomodulatory; secretory protein.

XX

OS Mycobacterium tuberculosis.

XX

PN WO200039301-A2.

XX

PD 06-JUL-2000.

XX

PF 23-DEC-1999; 99WO-US30975.

XX

PR 24-DEC-1998; 98US-0220416.

XX

PA (CORI-) CORIXA CORP.

XX

PI Skeiky Y;

XX

WPI; 2000-452399/39.

XX

N-PSDB; AAQ3601.

XX

Potentiating immune responses to antigens using specified Mycobacterium

tuberculosis proteins

XX

Claim 1; Fig 4B; 30pp; English.

XX

The Mycobacterium tuberculosis proteins encoded by AAQ3599-603

stimulate interleukin (IL)-12 and gamma-interferon production. A number

of cloned M. tuberculosis antigens were expressed as recombinant proteins

in Escherichia coli. After purification, these proteins were tested for

their ability to stimulate the production of IL-12 by a mouse macrophage

cell line, RAW264. The concentrations of IL-12 in RAW264 culture

supernatants were measured by an ELISA using an antibody to detect the

p40 component of the IL-12. Among the 18 proteins tested, only 2,

designated DpV and DPAS stimulated the production of IL-12. The

stimulatory activities of these proteins were not affected by the

inclusion of polymixin B in the cultures, which abrogated the IL-12

stimulatory activities of lipopolysaccharide, a polyclonal B cell

mitogen. Both DpV and DPAS are secretory proteins of M. tuberculosis.

A method of using the M. tuberculosis proteins to induce and potentiate

immune reactions to antigens is claimed.

XX

Sequence 302 AA;

X

Query Match

Best Local Similarity 100.0%; Score 88; DB 21; Length 302;

Matches 15; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

OY 1 CGNGKPSDLGNNLP 15

|||||

Db 254 cngkpsdlggnlp 268

OY 1 CGNGKPSDLGNNLP 15

|||||

Db 218 cngkpsdlggnlp 232

RESULT 5

AAQ11296

ID AAQ11296 standard; Protein; 338 AA.

XX

AC AAQ11296;

XX

DT 30-MAY-1991 (first entry)

XX

DE Recombinant M.tuberculosis 32kD antigen.

XX

KW tuberculosis; vaccine; BCG; antigen.

XX

OS Mycobacterium tuberculosis.

XX

FH Key Location/Qualifiers

FT Peptide 1..43

FT /label= signal peptide

FT 44..338

FT /label= tuberculosis 32kD anti

XX

PN EP419355-A.

XX

PD 27-MAR-1991.

XX

PF 19-SEP-1990; 90EP-0402590.

XX

PR 19-SEP-1989; 89EP-0402571.

XX

PA 19-SEP-1990; 90EP-0402590.

XX

PA (INNO-) INNOGENETICS NV SA.

XX

Content J, De Wit L, De Bruyn J, Van Voore

XX

WPI; 1991-088933/13.

XX

N-PSDB; AAQ11082.

XX

Polypeptide comprising recombinant polypeptic

peptide sequence(s) used for diagnosis and fo

XX

against tuberculosis

XX

Claim 3; Fig 5; 134pp; English.

XX

Polyclonal antiserum was raised in rabbits to

bovis BCG. The antiserum was then used to scre

recombinant DNA library constructed from genom

tuberculosis (Erdman strain). Positive clones

sequenced. The deduced amino-terminal amino a

mature protein corresponds to the same amino

MPB 59 antigen except for 3 amino acid differ

polypeptides of the invention contain at least

selected from the following (numbering refers

position 1 as -43, etc.): -30 to -1, 12 to 31

101 to 120, 175 to 194, 211 to 230 and 275 to

See also AAQ11081, AAQ11083, AAQ11086-90, AAQ

XX

SQ Sequence 338 AA;

XX

Query Match

Best Local Similarity 100.0%; Score 88; DB 12

Matches 15; Conservative 0; Mismatches

OY 1 CGNGKPSDLGNNLP 15

|||||

Db 254 cngkpsdlggnlp 268